Attorney Docket No.: 960296.95360

Applicant: Ronald T. Raines

Application No.: 09/234,028 Filed: 01/20/1999

Date of Office Action: 12 DEC 2008

Group Art Unit: 1652

Examiner: Richard G. Hutson

Date of Response: February 12, 2009

AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

- 1. (Currently amended) An oxidation-resistant engineered ribonuclease inhibitor (RI) variant selected from the group consisting of
- (i) [[an]] <u>a</u> RI variant differing from comprising the reference <u>sequence of SEQ ID</u> NO: 3, wherein the difference consists of <u>except for</u> an alanine <u>substitution of at least one</u> <u>cysteine</u> residue at <u>position positions</u> 95, 96, 329 or <u>and</u> 330; and
- (ii) [[an]] <u>a</u> RI <u>variant differing from comprising the</u> reference <u>sequence of SEQ ID</u> NO: 2, <u>wherein the difference consists of except for</u> an alanine <u>substitution of at least one</u> cysteine residue at <u>position</u> positions 324 or and 325,

the variant <u>RI</u> having a greater resistance to oxidation relative to the reference sequence for the variant <u>RI</u> and retaining its specificity and binding affinity to ribonuclease.

- 2. (Cancelled)
- 3. (Cancelled)
- 4. (Currently amended) The ribonuclease inhibitor variant RI of elaimClaim 1, wherein the difference alanine substitution inhibits the formation of a disulfide bond with an adjacent cysteine residue.

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5. (Currently amended) The ribonuclease inhibitor variant RI of claim 18 Claim 1, wherein the variant RI is 10 to 15 fold more resistant to oxidative damage than a native ribonuclease inhibitor an RI comprising the relevant reference sequence.

- 6. (Cancelled)
- 7. (Currently amended) The ribonuclease inhibitor variant RI of claim Claim 1, wherein the variant RI exhibits an *in vitro* inhibition of ribonucleolytic activity.
 - 8. (Cancelled)
- 9. (Currently amended) The ribonuclease inhibitor variant RI of claim Claim 18, having wherein the RI retains specificity and affinity of SEQ ID NO:3 for binding to angiogenin of the reference SEO ID NO:3.
 - 10. 17. (Cancelled)
- 18. (Currently amended) An oxidation-resistant ribonuclease inhibitor (RI) variant differing from comprising the reference sequence of SEQ ID NO: 3, wherein the difference consists of except for an alanine residue at position one or more of positions 95, 96, 329 or and 330.
- 19. (Currently amended) [[An]]<u>The</u> RI variant of Claim 18, wherein the residues at positions 329 and 330-being are alanine residues.

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- 20. (Currently amended) An oxidation-resistant ribonuclease inhibitor (RI) variant differing from comprising the reference sequence of SEQ ID NO: 2, wherein the difference consists of except for an alanine residue at position one or both of positions 324 or and 325.
- 21. (Currently amended) [[An]]<u>The RI variant</u> of Claim 20, <u>wherein</u> the residues at positions 324 and 325-being <u>are</u> alanine residues.
- 22. (Currently amended) [[An]]<u>The</u> RI variant of Claim 18, wherein the residues at positions 95 and 96 being are alanine residues.
- 23. (Currently amended) [[An]]<u>The</u> RI variant of Claim 18, wherein the residues at positions 95, 96, 329 and 330-being are alanine residues.